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Clarifying Differences Among Thrombolysis in Cerebral Infarction Scale Variants

Is the Artery Half Open or Half Closed?

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Background and Purpose—Although thrombolysis in cerebral infarction (TICI) 2b/3 has been regarded as a successful angiographic outcome, the definition or subclassification of TICI 2 has differed between the original (o-TICI) and modified TICI (m-TICI). We sought to compare interobserver variability for both scores and analyze the subgroups of the TICI 2.

Methods—Five readers interpreted angiographies independently using a 6-point scale as follows: grade 0, no antegrade flow; grade 1, flow past the initial occlusion without tissue reperfusion; grade 2, partial reperfusion in <50% of the affected territory; grade 3, partial reperfusion in 50% to 66%; grade 4, partial reperfusion in ≥67%; grade 5, complete perfusion. Readings using this scale were then converted into o-TICI and m-TICI score. Statistical analysis was performed according to TICI 2 subgroups.

Results—Interobserver agreement was good for the o-TICI and m-TICI scores (intraclass correlation coefficient, 0.73 and 0.67, respectively). Our grade 3 (partial reperfusion with 50% to 66%) occupied 19% of total readings, which would have been classified as grade 2a in o-TICI, but as 2b in m-TICI. The m-TICI was more likely to predict good clinical outcome than o-TICI (odds ratio, 2.01 versus 1.63, in reads with TICI 2b/3 versus 0/2a).

Conclusions—Both TICI scales showed good agreement among readers. However, the variability in partial reperfusion thresholds leads to different grading in ≈20% of cases and may result in significantly different rates of accurate outcome prediction. (*Stroke*. 2013;44:1166-1168.)

Key Words: interobserver variability ■ reperfusion ■ stroke ■ thrombolytic therapy ■ TICI

Originally proposed in 2003,¹ the thrombolysis in cerebral infarction (TICI) score has been widely used to assess angiographic findings after intra-arterial treatment of acute ischemic stroke. Numerous variations of the original TICI score have been introduced into the literature, often without clear justification for specific modifications or clear description of exact methodology.^{2,3} Furthermore, degree of interobserver variability for any variant of TICI remains poorly studied.^{4,5}

Many investigators have regarded TICI 2b/3 as a successful angiographic outcome; however, the definition or subclassification of TICI 2 differs between scores. TICI 2a is defined by <67% perfusion of the affected vascular territory in the original TICI (o-TICI).¹ The 2a subcategory in the modified TICI (m-TICI) is defined by <50% filling of the vascular area of the occluded artery and 2b as perfusion of ≥50% of the affected region.³

The degree of reperfusion after intra-arterial treatment as measured by TICI has been shown to be associated with clinical

outcomes and final infarct volumes.⁶ The clinical impact of using different thresholds within TICI 2 to define outcomes is unknown, but if a considerable proportion of patients who undergo revascularization are partially reperfused in the range of 50% to 66%, these differing thresholds could have a substantial impact on comparisons among treatments.

We sought to evaluate interobserver agreement of both TICI scores using our scale we devised, assigning those grades to both TICI scores and then analyzing the cases that would have been differentially categorized as TICI 2b/3.

Materials and Methods

After approval from the Mayo Clinic institutional review board, 146 angiographies of 73 patients who underwent intra-arterial treatment were randomly identified from the database of the institute. Consecutive anteroposterior and lateral angiographic images, from arterial to venous phase, were obtained in digital format and converted into a movie file. An evaluation file for online review was made, where preoperative and postoperative movies were compared.

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Five experienced readers (3 neurologists and 2 neuroradiologists) independently interpreted the images using our 6-point scale that was subsequently subdivided, as appropriate, to generate o-TICI or m-TICI scores. We defined o-TICI score as the literature,¹ and the m-TICI score is identical to the o-TICI, except that TICI 2 is subdivided at 50% rather than 67% of the territory. All readers were blinded to the clinical findings and to each other readings.

Our 6-point scale was defined as follows: grade 0, no antegrade flow; grade 1, flow past the initial occlusion but with no tissue reperfusion; grade 2, partial tissue reperfusion in <50% of the occluded artery territory; grade 3, partial reperfusion in 50% to 66% of the affected territory; grade 4, partial reperfusion in ≥67% of the affected territory; grade 5, essentially complete perfusion (please see the online-only Data Supplement). Reperfusion of the ischemic bed was assessed on the basis of the antegrade parenchymal blush rather than retrograde collateral blush. There was no formalized knowledge provided to the readers for this 6-point scale.

The intraclass correlation coefficient, as a parameter of interobserver agreement, was calculated with the 2-way random effects model, using IBM SPSS Statistics 19. Interpretation of intraclass correlation coefficient was as follows: poor, <0.40; fair-to-good, 0.40 to 0.75; excellent, >0.75. We evaluated the categorical variables with χ^2 test or Fisher exact test. Odds ratio was compared with reads of TICI 2b/3 versus 0/2a for good clinical outcome (modified Rankin Scale ≤2). Probability values <0.05 were considered statistically significant.

Results

Among 73 patients, mean age was 69.2 years (men:women = 50:33) and median National Institute of Health Stroke Scale Score at admission was 18. The occlusive vascular lesions were the middle cerebral artery (n=52), basilar artery (n=3), distal internal carotid artery (n=11), and proximal internal carotid artery (n=7). Forty patients (55%) received intravenous tissue plasminogen activator and 32 (44%) received intra-arterial tissue plasminogen activator. At 3 months, 24 patients (33%) had a good outcome (modified Rankin Scale, 0–2) and 22 (30%) had died (please see the online-only Data Supplement).

The intraclass correlation coefficient showed good between the o-TICI (0.73; 95% confidence interval, 0.65–0.95) and m-TICI (0.67; 95% confidence interval, 0.57–0.75). Overall, using our 6-point scale, 69 of 365 readings (19%) were in grade 3, that is, partial perfusion with 50% to 66% flow; these readings would have been classified as grade 2a in the o-TICI, but as 2b in the m-TICI (please see the online-only Data Supplement). In the o-TICI, 40% of total reads were TICI 2a and 33% as TICI 2b/3, whereas 21% corresponded to 2a and 52% to 2b/3 in the m-TICI ($P<0.0001$). There was also a significantly different clinical outcome (modified Rankin Scale ≤2) in the o-TICI versus m-TICI (15% versus 7% in TICI 2a and 13% versus 21% in TICI 2b/3; $P<0.005$). Compared with reads of TICI 0–2a, those with TICI 2b/3 in m-TICI (odds ratio, 2.06; 95% confidence interval, 1.31–3.27) were more likely to predict good outcome than o-TICI (1.63; 1.03–2.56).

Discussion

In the current study, we demonstrated that interobserver agreement was similar for both TICI versions. However, we found that a large fraction of cases would have been differentially classified as TICI 2b/3 based on whether the o- or m-TICI score had been applied. We also noted a significant difference in clinical outcome prediction when using the m-TICI as compared with the o-TICI score. Although these results

offer promise that the TICI score, when interpreted by experienced readers, performs well regarding interobserver variability, careful definition of terminologies and strict adherence to these definitions are crucial to ensure the reliability and reproducibility of the assessments.

Interobserver variability for angiographic scales focused on revascularization has been studied in relatively few publications. Qureshi et al⁵ reported that using 3 different scales, angiograms of 15 patients were graded by 3 neurointerventionists and showed good agreement among them. A more recent study⁴ proposed markedly lower reader agreement than ours, for reasons which are unclear.

Although several studies have defined successful reperfusion as TICI 2b or greater, they used various cutoffs for grade 2b, rendering comparisons across studies difficult or impossible. For example, in the Interventional Management of Stroke II Study⁷ with an overall recanalization rate of 64%, TICI 2b/3 was achieved in 32% of patients using the m-TICI score. Conversely, Imai et al² demonstrated TICI grade 2b/3 in 40% of cases in a study that used the o-TICI score and in which the total recanalization was 81%. These studies used primary clinical end points, but it is worth noticing that they relied on different definitions of TICI grade 2b. The definition of successful reperfusion in studies like these is paramount to our understanding of the correlation between angiographic results and clinical outcomes. One option to decrease the variability of the partial perfusion category and to permit a better comparison among reperfusion studies would be to define either TICI 2/3 or TICI 3 as successful reperfusion.⁸

Our study has several limitations. First, it was retrospective and encompassed a relatively small number of cases. Second, the occluded arteries were heterogenous, such as the middle cerebral artery, internal carotid artery, and basilar artery, which may affect the interpretation. Finally, it should be acknowledged that indirect evaluations using a 6-point scale might be different from directly applying either of the TICI scores.

Conclusions

Interobserver variability is good for both TICI versions. However, threshold variability used for the TICI partial perfusion category leads to different grading in ≈20% of cases and may result in significant differences of predicting good clinical outcome for the same angiographic data set. Future studies are needed to determine whether clinical outcome is better correlated with one or the other of the TICI versions.

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Disclosures

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ONLINE SUPPLEMENT

Clarifying differences among TICI scale variants:

Is the artery half open or half closed?

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Stroke, thrombolysis, observer agreement, intraclass correlation coefficient, TICI, reperfusion

Subjective code:

[44] Acute Cerebral Infarction, [73] Thrombolysis,

Tables

S 1. The 6-point scale and its transformation into both TICI scores

Interpretation	Current 6-point scale	Original TICI	Modified TICI
No antegrade flow	0	0	0
Flow past the initial occlusion but with no tissue reperfusion	1	1	1
Partial tissue reperfusion in <50% of the occluded artery territory	2	2A	2A
Partial tissue reperfusion in 50-66% of the occluded artery territory	3		2B
Partial tissue reperfusion in $\geq 67\%$ of the occluded artery territory	4	2B	
Essentially complete tissue reperfusion	5	3	3

**Assess the percent reperfusion of the ischemic bed based on the antegrade parenchymal blush (i.e., disregard parenchymal blush achieved through retrograde collaterals)*

S 2. Patients' demographics

Patients (n=73)	
Age, year (mean \pm SD)	69.2 \pm 11.9
Female (%)	33 (45%)
Hypertension (%)	59(81%)
Hyperlipidemia (%)	44(60%)
Diabetes (%)	21(29%)
Coronary artery disease (%)	28(38%)
Occlusive location (%)	
<i>MCA</i>	52(71%)
<i>BA</i>	3(4%)
<i>Distal ICA</i>	11(15%)
<i>Proximal ICA</i>	7(10%)
Initial NIHSS score	18 (IQR, 7-28)
tPA administration(%)	
<i>IV</i>	40(55%)
<i>IA</i>	32(44%)
IA mechanical thrombolysis (%)	62(85%)
<i>MERCI</i>	35
<i>Penumbra</i>	40
<i>Stent</i>	25
Clinical outcome at 3- month (mRS)	4(IQR, 1-6)

NIHSS, National Institutes of Health Stroke Scale; ICA, internal carotid artery; MCA, middle cerebral artery; BA, basilar artery; IV, intravenous; tPA, tissue-type plasminogen activator; IA, intra-arterial; IQR, interquartile range; mRS, modified Rankin Scale.

S3. Distribution of 365 reads and reads with good outcome using a 6-point scale

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Total	73(20%)	23(6%)	78(21%)	69(19%)	88(24%)	34(9%)
No. of Good outcome	11(3%)	8(2%)	24(7%)	28(8%)	38(10%)	11(3%)